

## PHYTOCHEMISTRY AND PHARMACOLOGICAL PROPERTIES OF ARAB MEDICINAL PLANTS

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### **Summary**

The number of patients seeking alternative and traditional Arab-Islamic medicine is growing exponentially. A very important factor that enhanced this increasing popularity and widespread use of Arab herbal medicines is not only equated to them being

inexpensive but for the better compatibility with the human body, minimal side effects, and thus better cultural acceptability, since they are prepared according to the principles of Greco-Arab and Islamic medicine (GAIM). Known throughout history “The Golden Era of the Islamic Civilisation” is famous for the generation of medical knowledge with well over a thousand years of Arab and Muslim experiences. At a parallel period, the west was stuck in the Medieval Dark Ages with brutal medical practices. Many medical innovations were introduced by Arab and Muslim physicians to the western world; these included but were not limited to: the discovery of the immune system, the introduction of microbiological science, and the separation of pharmacological science from medicine.

In modern day medicine several of the currently used synthetic drugs include a phytochemical prototype (e.g., aspirin; atropine; codeine; taxol). Black seeds, garlic, ginseng, olive oil, and pomegranate to name a few are gaining popularity amongst modern physicians and researchers alike. There is a growing body of evidence to show that pharmacological effects of medicinal plants are potentiated through synergistic mechanisms and/or combinations neutralizing side-effects. Safety of traditional herbal medicines is high due largely to the well documented traditional texts available to practitioners. This treasure trove of detailed experimental outcomes and scientifically proven plausible explanations are the reason life threatening results are rare which is comparable to the high numbers reported with a year on year increase within pharmaceutical products. This chapter will focus on efficacy and safety of commonly used Arab and Islamic medicinal plants and their active compounds.

## **1. Introduction**

Medicinal plants and their products are extensively used within indigenous healthcare systems in most Arab and Islamic countries. They have long been recognized for their therapeutic/prevention properties. For centuries, local cultures around the world have used herbal medicine to treat a myriad of ailments. By contrast, the rise of the modern pharmaceutical industry in the past century has been based on elucidation of individual active chemical compounds used with their precise modes of action. This approach has led to the development of hundreds of highly effective drugs that are widely used today. Regrettably modern medicine focuses on treating the symptom(s) as opposed to treating and healing the problem from the root, therefore, cures for complex human diseases with complicated causes, such as obesity, cancer, diabetes, autoimmune disorders and neuro-degenerative diseases (Saad et al, 2008; Saad et al, 2005; Saad and Said, 2011a) have been neglected.

According to the world health organization (WHO), about 80% of the world population relies upon traditional remedies for the health care of its people. Herbal medicine, also known as botanical medicine, herbalism, or phytotherapy, is the primary form of therapy in the well known traditional medical systems, namely, Ayurveda, Western, Chinese, Kampo, and GAIM (Figure 1) (Saad et al, 2008; Saad et al, 2005; Saad and Said, 2011a).

It is difficult to determine the precise numbers of plants that exist on earth, but as of 2016, there are thought to be about 375 thousand species of plants (Christenhusz and

Byng, 2016), of which only 15% have been evaluated to determine their pharmacological potential (Christenhusz and Byng, 2016). For therapeutic application, a specific part of the plant (aerial parts, roots, leaves, fruits, flowers, and seeds), is formulated into a suitable preparation e.g., tablets, teas, extracts, creams, or tinctures (Figure 2). While the plant kingdom continues to serve as an important source for chemical entities supporting drug discovery, the rich traditions of herbal medicine developed by trial and error on human subjects over thousands of years contain invaluable biomedical information just waiting to be uncovered using modern scientific approaches. Indeed, many of the currently used drugs are of herbal origin, certainly, about one quarter of these conventional drugs containing at least one active phytochemical. Some are made from plant extracts; others are synthesized to mimic a natural plant compound. The efficacy of herbal medicines is often described in very general terms, such as anti-inflammatory, anticancer, antiseptic, laxative, demulcent, antitussive, or carminative (Saad et al, 2008; Saad et al, 2005; Saad and Said, 2011a).

For some time the mono-substance therapy model or “one drug, one target, one disease” approach, has remained the conventional medical move towards the development of new drugs. However, over the last two decades, this therapy model has gradually shifted toward the adoption of combination therapies, in which multiple active components are employed. This shift has been partly driven by the limited effectiveness of the mono-substance therapy in managing chronic diseases as well as treatment resistance, and side effects of synthetic mono-drugs. Recent evidence (Saad, 2014; Pan et al, 2014) has demonstrated that combination therapy could provide greater therapeutic benefits to diseases such as cancer, obesity, acne, and diabetes, all of which possess complex etiology, pathophysiology and therefore are difficult to treat. Due to the fact that herbal-based medicines contain multiple phytochemicals, represent a promising alternative for the development of new drugs (Saad et al, 2008; Saad et al, 2005; Saad and Said, 2011a; Christenhusz and Byng, 2016; Saad, 2014).

It is a well-known fact with botanicals, that climatic conditions, different places as well as environmental factors may affect the concentration and chemical composition of therapeutic active phytochemicals; hence, it is not surprising that the folkloric use of a plant can vary in different geographical origins. It is therefore, vital in these instances that the dosage of the crude material is tested appropriately; especially where the therapeutic ratio is low (Therapeutic ratio is the ratio of the dose required for treatment to those causing toxic effects).

The widespread uses of selected sections of herbal products have brought concerns over the availability of wild plants for a growing market; it is feared that the limited supplies of known wild herbs are being threatened by overharvesting and habitat loss. The potential of isolating beneficial drugs from plants, however, has prompted large pharmaceutical companies to contribute to the conservation of the tropical rain forest (Saad et al, 2008; Saad et al, 2005; Saad and Said, 2011a; Christenhusz and Byng, 2016; Saad, 2014; Pan et al, 2014). However until this point is addressed with sincerity and not mere pledges for popularity vast sections of nature's apothecary will be lost forever.

Though yet to be proven, another concern surrounding herbal medicine is the fears over professionalism of practitioners, which in turn creates unnecessary apprehension over

the safety, quality, and efficacy of these products. In most Arab and Islamic countries, herbal-based products (e.g., whole plants, plant extracts, tinctures, and creams) are mostly sold over the counter and within the markets. Safety assessment of herbal-based remedies has often been neglected since over one thousand years of its prolonged and apparently harmless use, in addition to invaluable biomedical information gained, is usually considered sufficient evidence of their safety. Since herbal products are complex mixtures of active metabolites, once the crude material is tested appropriately using modern scientific approaches, any potential that they may cause toxic side effects such as hepatotoxicity and nephrotoxicity can be ruled out completely (Saad et al, 2008; Saad et al, 2005; Saad and Said, 2011a; Christenhusz and Byng, 2016; Saad, 2014; Pan et al, 2014).

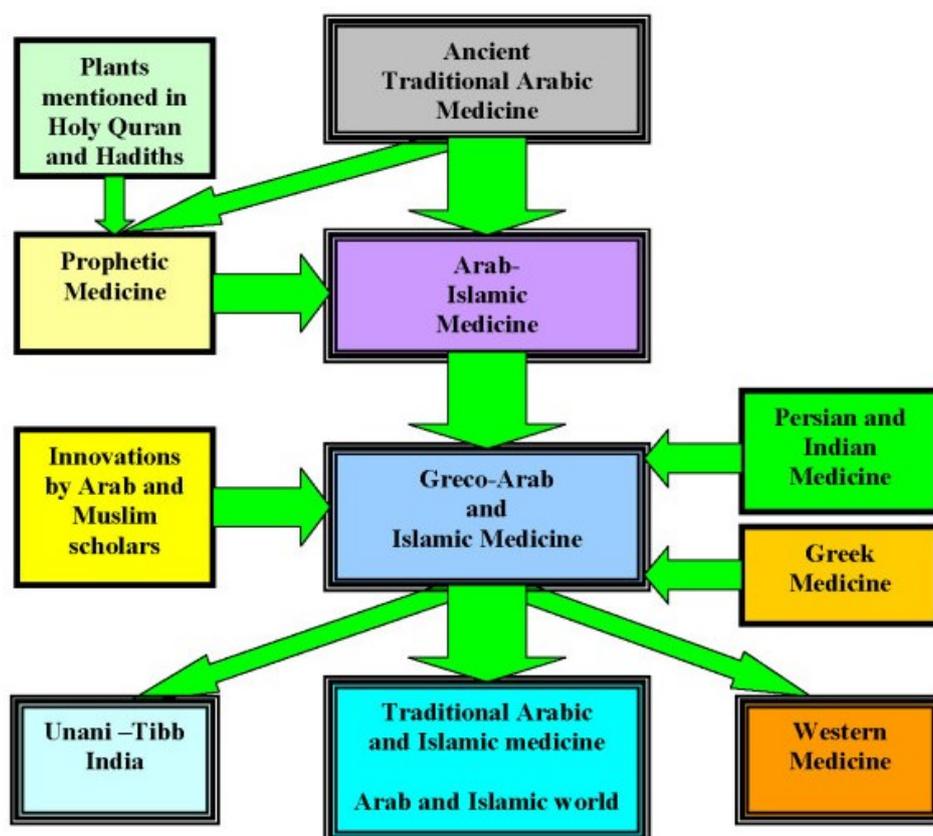


Figure 1. Development of Arab and Islamic herbal medicine

Ethnopharmacology has already played an important role in the development of conventional pharmaceuticals and is likely to play a more significant role in the future. There is no doubt that the use of herbal products will gradually be accepted within conventional medicine. Collaborations amongst ethnobotanists, biologists, ethnopharmacologists, physicians and phyto-chemists are essential for the fruitful outcome of medicinal plant research. The ethno-pharmacologists will play a more effective role in studying the rationale for the presence of different combinations of activities in individual medicinal plants. They will further, have knowledge and understand completely compound formulations, while the role of the phyto-chemists' will slightly shift towards the standardisation of medicinal plants and their products (Saad et al,

2008; Saad et al, 2005; Saad and Said, 2011a; Christenhusz and Byng, 2016; Saad, 2014; Pan et al, 2014).

## **2. Historical Aspect/Background**

GAIM has been used over hundreds of years for the management of disease, maintenance of health, and prolongation of life expectancy in Arab and Islamic countries (Saad, 2014; Pan et al, 2014; Pormann and Savage-Smith 2007; Morgan, 2007; Bilal and Jamal, 2007). Greco-Arab medicine, or Greco-Arab and Islamic medicine are terms that refer to medicine developed during the Golden Age of the Islamic civilization (seventh to fifteenth century), which extended from Spain to Central Asia and India. Scholars of the Muslim civilization translated and integrated scientific knowledge from the Greeks, Persians and Indian scripts into Arabic. Arab-Islamic medicine was not simply a continuation of Greek ideas, but rather a venue for innovation and change. This synthesis resulted in a richer and universal medical system, based on scientific roles and experimentation. For instance, the scholars and physicians of the Muslim World whose textbooks were used in European universities up to the sixteenth century such as: Al Tabbari (838-870); Al Razi (Rhazes, 846-930); Al Zahrawi (Albucasis 936-1013); Al-Biruni (973-1050); Ibn Sina (Avicenna, 980-1037); Ibn al Haitham (960-1040); Ibn Zuhr (Avenzoar, 1091-1161); Ibn al Nafees (1213-1288); Ibn al Baitar, (1197-1248); and Ibn Khaldun (1332-1395), are regarded as among the greatest medical authorities of the medieval world, or more correctly the Golden Age of Islamic civilization. The works of Ibn Sina and Al Razi on infectious diseases led to the introduction of quarantine as a means of limiting the spread of these diseases. Other physicians laid down the principles of clinical testing within humans, animals as well as drug trials, ultimately uncovering the secret of sight. The so called medieval GAIM laid the foundation of modern western medicine.

By the seventeenth century, the knowledge of herbal medicine was widely disseminated throughout Europe. In 1649, Nicholas Culpeper wrote *A Physical Directory*, and a few years later produced *The English Physician*. This respected herbal pharmacopeia was one of the first manuals that the layperson could use for health care, and it is still widely referred to and quoted today. The first U.S. *Pharmacopeia* was published in 1820 and became the legal standard for medical compounds in 1906. It included an authoritative listing of herbal drugs, with descriptions of their properties, uses, dosages, and tests of purity (Pormann and Savage-Smith 2007; Morgan, 2007; Bilal and Jamal, 2007; Saad and Said, 2011).

## **3. Revival of Interest in Phytomedicine**

Despite the incredible advances in both modern medicine and the pharmaceutical industry, traditional herbal medicine is considered a major healthcare provider around the globe, particularly in rural and remote areas. Large sections of the population in underdeveloped or developing countries still depend on such medicine for their primary healthcare. The world health organization (WHO) estimates that about 80% of the world population relies upon traditional remedies (mainly herbs) for the health care of its people. Herbal-derived active compounds represented about 80% of all drugs by the middle of the nineteenth century. Currently, at least 25% of sold drugs are plant-derived

compounds. In addition, about 75% of plants that provide active ingredients for prescription drugs came to the attention of researchers because of their use in traditional medicine. And among the 120 active compounds currently isolated from plants and widely used in modern medicine today, 80% show a positive correlation between their modern therapeutic use and the traditional use of the plants from which they are derived, despite the increase in side effects of synthetic drugs in comparison to their solely plant based counter-parts (Saad and Said, 2011; Saad, 2015; Jesse et al, 2009; Saad et al, 2006; Eko, 2014; Bandaranayake, 2006).

In line with the revival of interest in the old remedies, there is also research activity on medicinal plants particularly on the biological and pharmaceutical aspects and the impact factor of the journals publishing such research are growing with a rapid rate. One can imagine the popularity of herbal medicine in the west from the fact that an American Journal of Chinese Medicine exists in the literature. There is an increasing trend in North America and Europe to incorporate complementary and traditional medicine, particularly the herbs as an essential component in the medical curriculum.

The recent revival of public interest in herbal preparations has been attributed to several factors. These include, but are not limited to (1) the belief that herbal remedies are safe, (2) dissatisfaction with the results from conventional synthetic drugs, (3) relatively high prices of prescription of synthetic drugs, (4) claims on the efficacy of herbal-based remedies, (5) preference of consumers for natural therapies and a greater interest in alternative medicines, (6) belief that herbal products are superior to manufactured products, (7) research-based improvements in the quality, and safety of herbal-based preparations, and (8) a movement toward self-medication (Bilal and Jamal, 2007; Saad and Said, 2011; Saad, 2015; Jesse et al, 2009; Saad et al, 2006; Eko, 2014). In line with the revival of interest in the old remedies, there is also greater recognition of the scholarly work of the physicians of the olden days. As a result, many producers and health care institutions of Arab-Islamic herbal medicine are named after the famous scholars like, Al Razi, Ibn Sina, Al-Zahrawi, or Ibn-Al Baitar (Saad and Said, 2011; Eko, 2014; Bandaranayake, 2006; Brevort, 1998; Parle and Bansal, 2006).

#### **4. The Status of Herbal Medicine in the Mediterranean**

To evaluate the current status of Arab-Islamic herbal medicine, Saad and Said conducted a comprehensive survey covering most regions of historic Palestine (Parle and Bansal, 2006). Amongst others, they assessed the physicians' and people's attitudes towards herbal medicine, as well as their knowledge of specific therapies and the qualification of the traditional Palestinian herbal medicine practitioners. The main findings of this survey indicate: (1) that 87% of the interviewed persons prefer herbal-based medicines over synthetic drugs. About 30% of the asked people believe that all medicinal plants are safe, while 65.5% believe that not all plants are safe. About 93% of the interviewed persons do believe that herbal-based remedies are effective. About 95% of them were content with the result of medicinal plant treatments, and 53% confirm that the herbal treatment did indeed alleviate their ailment. Noteworthy, 72% do regularly use medicinal plants at home. Almost all interviewed people as well as traditional healers do support scientific research into the safety and efficacy of medicinal plants. (2) with regards to the status of qualifications, the authors found that

in parallel with the increased popularity of traditional medical systems over the last four decades, the qualifications of traditional Palestinian herbal medicine practitioners seems to be improving. About 62.5% of the interviewed practitioners claim to be highly successful in treating cases using only herbal-based remedies and about 53% of them claim to have an academic education and half of them have more than ten years' experience. About 70% of the interviewed practitioners report that they were able to identify the plants they use in nature and to identify different parts of the plant used to treat different diseases. Furthermore, most healers consider diet as part of the main treatment, and many of them consider media programs and written texts as an important source for their knowledge of herbal medicine. There are many books about herbal medicine on the market written in Arabic by non-specialized authors, who often employ texts by the famous Islamic physicians and herbalists such as Ibn al-Baitar and al-Antaki, which despite their wealth of knowledge maybe considered outdated to some. A possible error in solely relying on these texts is the likely misnaming of the plant species in question. It is well known that one plant can have many names, both locally and regionally; thus the recognition of the correct species can be exceptionally problematic, as, different plant species in many cases share the same common name. (3) with regards to physicians' attitudes toward herbal-based medicine; physicians were asked about their attitudes toward herbal-based preparations in general and their knowledge regarding these remedies. About 39.6% think that medicinal plants only treat very simple diseases, and only 20% of them are willing to recommend such therapies to patients with intractable or chronic diseases. Noteworthy, 43.8% would like to learn more about medicinal plants and their traditional applications, and 91% support scientific research to develop herbal medicines. About 83% believe that herb-based remedies can complement synthetic medicines, and 85% think that some herbs should be integrated with modern medicine. Furthermore, 54.2% think that their patients are interested in herbs. This study highlights the need for educational intervention and the importance of providing physicians with the ready access to evidence-based information regarding herb-based therapies (Saad and Said, 2011b).

## **5. Safety Monitoring and Regulatory Status of Herbal Medicines**

The observed worldwide popularity in the acceptance and utilization of herbal remedies and related products continue to assume exponential increase. Due to the belief in these medical systems which have been used for hundreds of years, a natural product-based diet and herbal-based remedies are considered safe because they are derived from "natural" sources. The reality is that "safety" and "natural" are not synonyms. It is therefore necessary that, regulatory policies on herbal medicines and products are standardized and strengthened on both national and international levels. Relevant regulatory authorities in different countries of the world need to be proactive and continue to put in place appropriate measures to protect public health by ensuring that all herbal medicines approved for sale are safe, of suitable quality and free of potential contaminants (Saad et al, 2008, 2005; Saad and Said, 2011a; Christenhusz and Byng, 2016; Saad, 2014; Pan et al, 2014; Pormann and Savage-Smith 2007).

Although the assessment of the safety of herbal medicines has become an important issue for consumers, regulatory authorities, and healthcare professionals alike, analysis of adverse events related to the use of these products is much more complex than in the

case of conventional pharmaceuticals. It is also recognized that the evaluation of safety is complicated by a number of factors such as the geographical origin of plant material, different processing techniques, route of administration, and compatibility with other synthetic medicines. In addition, a single herbal medicine or medicinal plant may contain hundreds of natural constituents, and a mixed herbal medicinal product may contain several times that number. Furthermore, there is lack in knowledge and/or poor emphasis on the importance of taxonomic botany and documentation by most manufacturers of herbal medicines. This indeed poses peculiar challenges during identification and collection of medicinal plants used for herbal remedies. In order to eliminate the confusion created by the common names, it is necessary to adopt the most commonly used binomial names (including their binomial synonyms) and collating them together for medicinal plants. For example, *Artemisia absinthium* L., which contains an active narcotic derivative and is capable of causing CNS disorders and generalized mental deterioration, has at least 11 different common names. Seven of the common names bear no resemblance to its botanical name. This explains why it is important to provide the exact scientific name of the plant, the plant part used, and the name of the manufacturer when reporting adverse drug reactions of herbal medicines. Therefore, effective monitoring of the safety of herbal medicines will require effective collaborations between botanists, phytochemists, pharmacologists, and other major stake-holders (Saad and Said, 2011a&b; Saad et al, 2006; WHO, 2005; Kim et. al., 2012).

The increasing use of herbal medicines and products in developed countries coupled with the absence or weak regulation of these products in most countries as well as the occurrence of high-profile safety concerns, have all increased the need to monitor safety and deepen the understanding of possible side effects, and the potential benefits associated with the use of herbal medicines. Adverse events arising from the consumption of herbal medicines are attributable to several factors among which include, the contamination with toxic or hazardous substances, use of the wrong species of plant/misidentification of the plant, adulteration of herbal products with other, undeclared medicines, over dosage, misuse of herbal medicines by either healthcare providers or consumers and the use of herbal medicines concomitantly with other synthetic medicines (Saad and Said, 2011a&b; Eko, 2014; Kim et. al., 2012; Rodrigues and Barnes, 2013).

Safety monitoring and regulatory status of herbal medicines vary from one country to another. Depending on the regulations applying to foods and medicines in different countries, a single herb may be considered as a diet, a functional diet, a dietary supplement, or a herbal medicine. This introduces serious difficulty in the definition of the concept of herbal medicines for the purposes of national drug regulation while at the same time also confuse patients and consumers. In the United States, for example, natural products are regulated under the Dietary Supplement Health and Education Act (DSHEA) of 1994 (U.S. Food and Drug Administration, 2012). By definition, a dietary supplement is a product that is ingested and is intended to supplement the diet and contains a “dietary ingredient.” The dietary ingredients in these products may include vitamins, minerals, herbs, or other botanicals (U.S. Food and Drug Administration, 2011). Under the DSHEA, additional toxicity studies are generally not required if the herb has been on the market prior to 1994 (National Institute of Health (NIH) Office of

Dietary Supplements, 2011). In this regard, the FDA bears the burden to prove that a herbal medicinal product or “dietary ingredient” is toxic or not safe for use. A major additional challenge in many countries is the fact that the regulatory information on herbal medicines is often not shared between the regulatory authorities and the safety monitoring centers (Saad and Said, 2011b; Saad et al, 2006; WHO, 2005; Kim et. al., 2012).

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